SUPPORT FOR THE AMENDMENTS

Claims 23, 24, and 26 were previously canceled.

Claim 19 is canceled herein.

Claims 13 and 16 have been amended.

Claim 28 has been added.

The amendment of Claim 13 is supported the claim as previously presented and throughout the specification as filed. The amendment of Claim 16 are supported by previously pending Claim 19 and the specification as filed, for example at page 22, line 11 to page 28, line 3 (Example 1), in particular page 33, line 11 to page 25, line 9. New Claim 28 is supported by the specification as filed, for example at page 67, line 3 to page 71, line 3 (Example 8).

No new matter is believed to have been entered by these amendments.

REMARKS

Claims 1-18, 20-22, 25, 27, and 28 are pending in the present application. Claims 13-18, 20-22, 25, 27, and 28 read on the elected invention and are currently under examination by the Examiner in the present application (Claim 28 is newly added)

At the outset, Applicants wish to thank Examiner Fronda for the helpful and courteous discussion with their undersigned Representative on February 9, 2006. During this discussion, several amendments and remarks were discussed to address the outstanding rejections. The content of this discussion is believed to be reflected in the amendments and remarks herein. Reconsideration of the outstanding rejections is respectfully requested.

The rejection of Claims 13-22, 25, and 27 under 35 U.S.C. §112, first paragraph (written description), is respectfully traversed.

In the outstanding Office Action the Examiner alleges that the claimed invention fails to meet the written description requirement of 35 U.S.C. §112, first paragraph, because the terms "phosphoglucose isomerase," "phosphoribosyl pyrophosphate amidotransferase," and "phosphoribosyl pyrophosphate synthetase" do not define any structural features and amino acid sequences commonly possessed by each genus. Applicants disagree with this assertion by the Examiner.

In referring to Claim 13, it is clear that the scope of the recited enzymes is limited to a microorganism belonging to the genus *Escherichia*. As evidenced by that the sequences underlying the terms "succinyl-adenosine monophosphate synthase, purine nucleoside phosphorylase, adenosine deaminase, inosine-guanosine kinase, guanosine monophosphate reductase, 6-phosphogluconoate deydrase, phosphoglucose isomerase, adenine deaminase,

and xanthosine phosphorylase" were known in the art at the time of the present invention, Applicants **submit herewith** Blattner et al, *Science* 277, 1453-1462 (1997), which placed the public in possession of the complete genomic nucleotide sequence of E. coli. Further, the polynucleotide and encoded polypeptide sequences were publicly available via the GenBank sequence data based as of the date of the present invention. Thus, the sequences of the present invention were *per se* known in the art as of the date of the present invention.

Indeed, the Courts have recently held that the "written description" requirement must be applied in the context of the particular invention and the state of the knowledge in the art (*Capon v. Eshhar*, 418 F.3d 1349, 76 USPQ2d 1078 (Fed. Cir. 2005), copy **submitted herewith**). In *Capon*, the Court held that the Board erred in holding that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known. The *Capon* Court further stated that when the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh. Therefore, where a person experienced in the field of this invention would know that the DNA of the claims is well-known, *there is no requirement to once again set forth these sequences.*

Further, as in *Capon*, the present invention is not in discovering which DNA sequences correspond to the various recited genes, as these sequences were available in the prior art as of the date of the present invention. Instead the present invention lies in the carefully orchestrated expression of the recited genes to achieve a novel result.

The "written description" requirement states that Applicants must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution. The present invention does not concern the discovery of gene

function or structure as in *Lilly* that, as in *Capon*, is improperly relied upon by the Examiner in the present application. The sequences recited in the claims correspond to those that are of known structure and function. As such, this ground of criticism with respect to written description is not appropriate for the reasons promulgated by the *Capon* Court and should be withdrawn.

Acknowledgement that this ground of rejection has been withdrawn is requested.

The rejection of Claims 16 and 19 under 35 U.S.C. §112, first paragraph (enablement), is obviated by amendment.

At the outset, Applicants note that Claim 19 has been canceled. Claim 16 has been amended based on Example 1 at page 22, line 11 to page 28, line 3, in particular at page 33, line 11 to page 25, line 9. Applicants submit that the Claim 16 finds enabling support in Example 1 and, therefore, this rejection is no longer tenable.

Withdrawal of this ground of rejection is requested.

The rejections of: (a) Claims 13 and 27 under 35 U.S.C. §103(a) over Mascarenhas et al in view of Gelpi; (b) Claims 14, 15, and 17-21 under 35 U.S.C. §103(a) over Mascarenhas et al in view of Gelpi and Neuhard et al; (c) Claim 22 under 35 U.S.C. §103(a) over Mascarenhas et al in view of Gelpi, Neuhard et al, and Rolfes et al; and (d) Claim 25 under 35 U.S.C. §103(a) over Mascarenhas et al in view of Gelpi and Accession No. P09452, are obviated by amendment.

In the Office Action the Examiner asserts that it would have been obvious to the skilled artisan to modify the process taught by Mascarenhas et al by collecting the produced purine nucleoside and subsequently subjecting it to liquid chromatography-mass

spectrometry analysis as taught by Gelpi to identify and measure the amount of purine nucleoside produced. Despite the fact that Mascarenhas et al fail to disclose the effect of deletion of phosphoglucose isomerase on tryptophan biosynthesis and are silent with respect to production and collection of a purine nucleoside, the Examiner holds fast to the foregoing position.

During the February 9, 2006, discussion with the undersigned, the Examiner clarified the prior art rejections. The Examiner indicated that these rejections are necessitated by the fact that Claim 13 reads on recovery of purine nucleosides from a microorganism that expresses *basal* levels of the same. Therefore, the Examiner alleges that Mascarenhas et al is properly cited since every microorganism must inherently produce purines to be viable.

In view of the foregoing, Applicants have amended Claim 13 to require *enhanced* production of purine nucleosides as compared to the uninhibited microorganism. In view of this amendment, Applicants submit that the prior art rejections are no longer tenable. Specifically, Applicants submit that none of Mascarenhas et al, Gelpi, Neuhard et al, Rolfes et al, or Accession No. P09452 disclose or suggest enhanced production of purine nucleosides, much less modification of the microorganism belonging to the genus *Escherichia* to block a reaction branching from purine nucleoside biosynthesis and leading to another metabolite in said microorganism as presently claimed.

In view of the foregoing, Applicants request withdrawal of these grounds of rejection.

The objection to Claim 13 due to the presence of a typographical error is obviated by amendment. Applicants have corrected the spelling of the term "phosphoglucose." As such, withdrawal of this objection is requested.

The objection of Claims 13-22 and 25 as reciting non-elected subject matter is traversed.

Claim 13 provides a method for producing a purine nucleoside by fermentation by culturing a microorganism in a culture medium to produce and accumulate the purine nucleoside in the medium, and collecting the purine nucleoside, where the microorganism belongs to the genus *Escherichia* and is modified to block a reaction branching from purine nucleoside biosynthesis and leading to another metabolite in said microorganism, where the microorganism produces an amount of purine nucleoside that is greater than the amount produced by the corresponding wild type microorganism, and where the reaction is catalyzed by an enzyme selected from the group consisting of succinyl-adenosine monophosphate synthase, purine nucleoside phosphorylase, adenosine deaminase, inosine-guanosine kinase, guanosine monophosphate reductase, 6-phosphogluconoate deydrase, phosphoglucose isomerase, adenine deaminase, and xanthosine phosphorylase.

On June 21, 2001, the Examiner required an election of single disclosed species from the members of the Markush group above. In electing phophoglucose isomerase, Applicants directed the Examiner's attention to the fact that the Examiner's statement that the species lack unity of invention is incorrect (see Response to Restriction and Election of Species Requirement filed July 13, 2001). Specifically, Applicants noted that

> According to the PCT administrative instructions in MPEP, Annex B, Part I (f), the requirement of the same special technical feature as defined in PCT Rule 13.2 is considered to be met when the alternatives of a Markush group are of similar nature. Here, the enzymes have a common activity because they catalyze the reaction branching from the purine nucleoside biosynthesis. In addition, the compounds of the Markush group belong to a recognized class of chemical compounds in the art to which the invention pertains. All compounds are enzymes.

Moreover, Applicants noted that a search of all the claims would not impose a serious burden on the Office (MPEP §803). Applicants further noted that the International Searching

Authority had already examined all of the claims (including the species contained therein) together. Therefore, the Office has not applied the same standard of unity of invention as the International Preliminary Examination Authority (see the International Preliminary Examination Report). The Authority did not take the position that unity of invention was lacking in the International application and examined all claims together. Applicants note that PCT Article 27(l) states:

> No national law shall require compliance with requirements relating to the form or contents of the international application different from or additional to those which are provided for in this Treaty and the Regulations.

Despite the foregoing, the Examiner maintained the Election of Species Requirement for the members of the Markush group.

On March 22, 2004, Applicants filed a Petition requesting reconsideration of the Restriction and Election of Species Requirement. The Petition's Examiner granted-in-part Applicants Petition by merging original Groups I-VI into new Group I and maintaining original Group VII as new Group II. In addition, the Petition's Examiner maintained the Election of Species Requirement.

The basis for maintaining the Election of Species Requirement is that: (1) burdensome search is not a requirement for restriction under lack of unity of invention, (2) the position taken by the International Authority holding unity to be satisfied is irrelevant to the U.S. Patent Office, and (3) the species election is proper because "all the enzymes do not share a common structure and at least one Markush alternative is not novel over the prior art. Specifically, Seeger et al... teach the enzyme xanthosine phosphorylase as claimed and Mori et al... teach the enzyme inosine-guanosine kinase as claimed."

Applicants disagree with at least positions (2) and (3) set forth by the Petition's Examiner.

With respect to position (2), the Office is again referred to PCT Article 27(1), which states:

> No national law shall require compliance with requirements relating to the form or contents of the international application different from or additional to those which are provided for in this Treaty and the Regulations.

As is already of record, the International Preliminary Examination Authority already reviewed the very claims that the U.S. Patent Office issued a Restriction and Election of Species Requirement over. The International Preliminary Examination Authority, examining under the unity of invention standard, did not take the position that unity of invention was lacking in the International application and examined all claims together. However, the U.S. Patent Office, supposedly applying the same rules, found unity lacking. How then can this be reconciled? The only rationale is that the U.S. Patent Office has not applied the same standard of unity of invention as the International Preliminary Examination Authority. Applicants kindly request that the U.S. Patent Office reconsider its position with respect to unity of invention.

Further, with respect to position (3), Applicants submit that the Office has improperly applied the standard set forth in Annex B of the Administrative Instructions with respect to the Markush-type claims. PCT administrative instructions in the MPEP, Annex B, Part 2(f) specify that when examining Markush-type claims: "the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2, shall be considered to be met when the alternatives are of a similar nature." MPEP, Annex B, Part 2(f) further states:

(i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) all alternatives have a common property or activity, and

(B) (1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or

(B) (2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

ii) In paragraph (f)(i)(B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together.

(iii) In paragraph (f)(i)(B)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

As stated above, the Petition's Examiner previously held that the members of the Markush group fail to meet the unity of invention standard, because all members fail to share a common structure. However, from the foregoing, it is clear that not all members of a Markush group need a common structure. Unity is also present where "all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains."

In the present application, each member of the Markush group is recognized by the skilled artisan to be members of a recognized class of chemical compounds in the art to which the invention pertains as each of the members are enzymes that catalyze reactions that branch from the purine nucleoside biosynthetic pathway. Further, Applicants submit that

based on the disclosure in the present specification, the skilled artisan would expect that each of the listed enzymes would behave in the same way in the context of the claimed invention.

Moreover, with respect to novelty, Applicants note that each of the cited references merely disclose the enzyme *per se*. None of these references disclose or suggest the use of an Escherichia microorganism in which the reaction catalyzed by the enzyme is inhibited, much less that the inhibition thereof is used for the enhanced production of a purine nucleoside. As stated above, novelty of the present invention does not lie in the identity of the sequences *per se*, but rather in the method and novel effect flowing therefrom. Therefore, the cited references do not show that any of the Markush alternatives is not novel when in the context of the claimed invention.

To this end, novelty should be determined based on whether the claimed invention of using the enzyme is novel or not. In other words, novelty cannot be considered by extracting a single element from the claim and looking at this element of isolation. Novelty must be determined contextually. If the enzyme *per se* must be novel irrespective of the context of the claimed invention, a Markush expression could not be allowed in any invention that is directed to a new combination of known components. For example, if a claim were presented to an apparatus sealing automotive glass and an element of the claim were a fastener selected from the group consisting of a nail, a screw, a tack, and chewing gum, it would be unreasonable for the Office to say that these Markush members are not capable of being examined together because each of a nail, a screw, a tack, and chewing gum were known in the art. Certainly the proper way to examine this is whether these members were used in the appropriate context. To examine novelty any other way would be unreasonable, contrary to administrative efficiency, and inconsistent with the PCT administrative instructions.

Further, with respect to administrative efficiency, in an attempt to justify the recent proposed rule change package with respect to Continuation Practice (71 *Fed. Reg.* 48 (03 January 2006)), Director Dudas recently pointed to continuation applications as the primary cause of the backlog at the U.S. Patent Office. Director Dudas blamed the filing of multiple applications for the same invention as leading to an increase in inefficiency as Examiners are being forced to reexamine applications that have previously been filed, searched, and examined. However, the Office's position in this application seems to feed directly into this perceived problem. In this case, requiring Applicants to file multiple applications for the same invention would be a needless burden upon the Office resources.

In view of the foregoing, Applicants submit that the Election of Species Requirement is improper and should be withdrawn. In view thereof, no further amendment is believed to be necessary and this ground of objection should be withdrawn.

Applicants submit that the present application is in condition for allowance. Early notification to this effect is respectfully requested.

Respectfully submitted,

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